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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,874	01/14/2002	Hendrick Jan Houthoff	570-28 PCT/US/DIV	6706
23869	7590	12/03/2003	EXAMINER	
HOFFMANN & BARON, LLP			RILEY, JEZIA	
6900 JERICHO TURNPIKE			ART UNIT	
SYOSSET, NY 11791			PAPER NUMBER	

1637

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/047,874

**Applicant(s)**

HOUTHOFF ET AL.

**Examiner**

Jezia Riley

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 23-137 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23-29, 33-51, 55, 59-75, 79, 83-101, 105, 109-124 and 128-137 is/are rejected.
- 7) ☒ Claim(s) 30-32, 52-54, 56-58, 76-78, 80-82, 102-104, 106-108 and 125-127 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_ 6) ☐ Other: \_\_\_\_

## DETAILED ACTION

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23-26, 28, 29, 34-46, 48-51, 59-71, 73-75, 84-96, 98, 100, 101, 109-121, 123, 124, 129-137 are rejected under 35 U.S.C. 102(e) as being anticipated by van den Berg et al. (5,580,990).

Van den Berg discloses a compound with the formula {Pt.II (w)(x)(y)(z)} or {Pt.IV (u)(v)(w)(x)(y)(z)} with the structural formula 1 or 2 in which u, v, w, x, y and z represent whether or not the same whether or not interconnected ligands, from which at least one is a leaving ligand and at least one of the remaining ligands represents a detectable marker group. Such a compound which is novel per se, and on the one side is provided with a directly or indirectly detectable marker group, as for instance a hapten, fluorescein or rhodamine and on the other side is provided with a suitable leaving group, is an especially suitable and novel DNA label with the general indication PtM (Pt stands for platinum and M stands for marker group) with unique properties. The detectable marker group is fluorescein, rhodamine, 7-amino-3-methylcoumarin-3-acetic acid, biotin

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or other hapten, digoxigenin, a radioactive moiety, or an immunohistochemically detectable moiety,

For it appeared, that such a compound adheres spontaneously and irreversibly to DNA in aqueous medium. Further, the thus labelled DNA may be separated from the redundant compound with the formula 1 or 2 by alcohol precipitation. An important advantage is, that the thus labelled DNA may be detected immediately after hybridization by means of a fluorescence microscope or indirectly with one of the known immunohistochemical staining techniques. (col. 1-2) .

The preferred compound, is prepared by conversion of fluorescein-N=C=S with  $\text{CH}_3\text{NH}_2$  in water, after which the mentioned fluorescein-NH(CS)NHCH<sub>3</sub> is precipitated from the solution by acidifying to a pH of 2-3, after which the precipitate obtained is suspended in water and the pH of the suspension is brought to a value of 10-11 by addition of a base, providing a bright yellow solution, to which solution {Pt(ethylenediamine)(Me<sub>2</sub>SO)Cl} in water is added and the reaction mixture is stirred at room temperature in the dark, after which the non-reacted fluorescein-NH(CS)NHCH<sub>3</sub> is precipitated by acidification and filtered and finally the filtrate is freeze-dried yielding {Pt(ethylenediamine)(Me<sub>2</sub>SO)(fluorescein-NH(CS)NHCH<sub>3</sub>)} (PtF). (col. 3-4).

As further advantage may be mentioned, that for specific purposes (for instance extra sensitive in situ hybridization of RNA) a radioactive (<sup>14</sup>C or <sup>35</sup>S)-platinum-containing compound according to the invention may be applied as simple and fast (non-enzymatic) labelling of probes, followed by direct detection by means of

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autoradiography. (col.2). Subsequently, the reference extends to a diagnostic kit for use in the detection of viruses, bacteria, parasites, genetic deviations, gene expression, which kit comprises the Pt-containing compound.

Claims 23-29, 33-51, 55, 59-75, 79, 84-101, 105, 109-124, 128-137 are rejected under 35 U.S.C. 102(e) as being anticipated by Houthoff et al. (5,985,566).

Houthoff discloses platinum-based compounds which are controllably and substantially irreversibly reactive with biological molecules, including methods of making such compounds and methods for their use. The invention further provides platinum-based compounds useful for detecting the presence of biological target molecules, as well as methods for employing such compounds. The invention further includes diagnostic kits containing platinum-based compounds of the invention which permit the labeling of biomolecules, and the detection of target biomolecules in a variety of testable systems.

Houthoff provides detectable probe compounds having the structure as shown in col 2, and col. 5-6, wherein: Pt is a platinum atom, PROBE is a probe biomolecule for associating to a target biomolecule, M is a detectable marker moiety, and X and Y are stabilizing substituents. Preferably, the PROBE moiety is a biomolecule such as a nucleic acid, a protein, or a lipid. More preferably, the PROBE moiety is a biomolecule selected from among nucleotides, nucleosides, modified nucleotides, modified nucleosides, oligonucleotides, polynucleotides, amino acids, modified amino acids,

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oligopeptides, polypeptides, proteins, glycoproteins, lipoproteins, steroids, fatty acids, and the like.

The detectable marker moiety (M) may include any moiety known in the art which is detectable, either directly, e.g., a fluorescent compound, or indirectly, e.g., an enzyme which cause a color change in a medium. Preferably, the detectable marker moiety is selected from among radioactive labels, enzymes, specific binding pair components, colloidal dye substances, fluorochromes, chromogens, reducing substances, colored latex sols, digoxigenin, metal sols, particulate sols, dansyl lysine, antibodies, protein A, protein G, and the like. Still more preferably, the detectable marker moiety is a fluorescent group chosen from among compounds such as fluoresceins, eosins, trisulfonylpyrenes, rhodamines, digoxigenins, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes, and derivatives thereof. Other more preferred M moieties include binding pair components chosen from among biotins, iminobiotins, avidins, streptavidins, biocytins, and derivatives thereof.

The stabilizing substituents X and Y may be the same or different, and are substantially unreactive with biomolecules of interest. In a preferred embodiment, X and Y are interconnected, forming a stabilizing bridge moiety. Preferred stabilizing bridge moieties include aliphatic diamines, more preferably aliphatic diamines having between 2 and 6 carbon atoms. A highly preferred stabilizing bridge moiety is ethylenediamine.

The reactive moieties A and B are preferably the same. Moreover, A and B are preferably selected from among halogens, NO<sub>3</sub>, and SO<sub>3</sub>. One or more of these

markers M may be attached to the platinum compounds either directly or through spacer arms (preferably polylysine).


Claims 30-32, 52-54, 56-58, 76-78, 80-82, 102-104, 106-108, 125-127 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 703-305-6855 (after 1/20/04, 703-272-0786). The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Friday, November 28, 2003



**JEZIA RILEY**  
**PRIMARY EXAMINER**